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droxide, and the lysine as picrate. The residual solution contained an amount of non-amino nitrogen corresponding approximately to that determined by Van Slyke's method in excess of the arginine and histidine non-amino nitrogen.

Attempts to crystallize the free base or its derivatives have been successful only with the phosphotungstate. Recrystallization of the phosphotungstate yields a product in which the ratio, *Total N : Amino N* = 2 : 1. The free base prepd. from the recrystallized phosphotungstate is hygroscopic, and decomposes slowly when dried at 100°. It does not appear to be a peptide, for the ratio of amino to total nitrogen is not increased by boiling 40 hours with 20 per cent hydrochloric acid, nor by heating 8 hours in a bomb tube at 125° with 25 per cent sulfuric acid. We are engaged in the preparation of larger amounts of the substance in the hope of determining its structure.

[1] Literature quoted by D. D. Van Slyke, *J. Biol. Chem.*, **10**, 1911 (15).

[2] Koessler, K. K., and Hanke, M. T., *J. Biol. Chem.*, **39**, 1919 (497).

GENETICAL AND CYTOLOGICAL PROOF OF NON-DISJUNCTION OF THE FOURTH CHROMOSOME OF DROSOPHILA MELANOGASTER[1]

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Communicated by T. H. Morgan, March 18, 1921

A mutant type of *D. melanogaster* known as "Diminished" gave genetical results which proved the involvement of a "deficiency,"[2] i.e., a multilocal loss of genes, in the chromosome corresponding to the "fourth linkage group"[3,4] (see section I). Further exceptions to normal inheritance showed that non-disjunction[5] of this chromosome had occurred giving rise to (Diminished) individuals lacking one member of the fourth-chromosome pair (see section II). The deficiency in this case consisted therefore in the loss of an entire chromosome. The haploid nature of Diminished was then proved cytologically: it was found that in the cells of Diminished individuals only one small round chromosome was present instead of a pair (section III). This finding demonstrates the correctness of the view that the carrier of the genes of the fourth linkage group is the small round chromosome. A positive direct proof is provided that a particular autosome is the carrier of the genes of particular non-sex-linked Mendelian characters.

I. The features that in the aggregate prove that a deficiency is involved are:

(1) A definite complex of mutant characters: Diminished differs somatically from the wild-type in many characters, among which the principal are: smaller size throughout; bristles relatively shorter and more slender; body-color paler; thorax-pattern darker; eyes larger and roughish, somewhat denuded of hairs; aristae reduced or absent; wings slightly spread, blunter, and less clear in texture.

(2) Low productivity.

(3) Frequent stirility.

(4) Dominance.

(5) Heavy mortality: Outcrosses of "heterozygous" Diminished to wild-type gave an extremely variable proportion of Diminished; the bulk of the cultures ranged from 20 to 50 per cent, with a mean value of 34.5 (1772 Dm: 3366 wild-type). Since the Diminished offspring were expected to be as numerous as the wild-type, the mortality of the Diminished is very high, viz. 47%.

(6) Delayed hatching: Diminished adults begin to emerge from the pupa cases four or more days later than wild-type sibs. The delay is apparently due to a slow metamorphosis.

(7) Lethal when "homozygous:" When "heterozygous" Diminished was inbred there were 139 Diminished to 100 wild-type (1079 : 775). The expectation for such inbreeding, on the basis that "homozygous" Diminished is lethal and that mortality of the "heterozygous" Diminished is the usual 47%, is 106 : 100, which is somewhat under the observed ratio. The mortality of Diminished is extremely variable, and a mortality of 31% would give the observed ratio. Further evidence in favor of the lethal view is the fact that continued inbreeding did not increase the percentage of Diminished; also no Diminished individual was found that gave all Diminished offspring upon outcrossing.

(8) Inheritance as member of the fourth chromosome:

(*a*) The Diminished mutant is not due to a change in the first, second, or third chromosomes: Reciprocal crosses gave like results, and outcrosses of Diminished male to wild female gave Diminished offspring among the sons, so the Diminished is known to be neither cytoplasmic nor sex-linked in inheritance. Male back-cross tests with such well-known second-chromosome mutants as Star and black, and third-chromosome mutants, such as Dichaete, Hairless, pink and ebony, showed free assortment of these mutants with Diminished. Since there are only four chromosome pairs in *D. melanogaster* the above evidence proves that Diminished is caused by a change in the remaining or "fourth" chromosome.

(*b*) That Diminished is due to a fourth-chromosome change might be proved by means of male back-cross tests with the known fourth-chromosome recessive mutants bent and eyeless. But when crosses of Diminished to bent and to eyeless were made in order to secure the necessary heterozygotes, it was found that all the F_1 flies that were Diminished were at the same time bent or eyeless, respectively. This fact made the intended back-cross tests both impossible and unnecessary. Crosses of bent, or of eyeless, to wild and to other mutants give only not-bent or not-eyeless progeny in F_1, while, on the other hand, crosses of Diminished to a great variety of recessives in the first, second, and third chromosomes have never given F_1 Diminished that showed any of those recessives. The fact that the Diminished allows "pseudo-dominance" of two dissimilar non-allelomorphic fourth-chromosome recessives proves that Diminished is due to a fourth-chromosome change, and one of a definite known class—that of "deficiencies."

(9) Pseudo-dominance of recessives in the affected section: Pseudo-dominance, such as found for the recessives bent and eyeless with Diminished, had already been met with in such cases as forked with Bar-deficiency,[1] vermilion with vermilion-deficiency,[6] and facet, abnormal and the white allelomorphs with Notch-deficiencies.[7] The explanation in these cases is that the section of chromosome from forked to bar inclusive, the section containing the vermilion locus, and the section from white to facet and abnormal inclusive, had been lost, or transformed in such a way as to have lost the normal action of its genetical materials. All previously enumerated features of Diminished are explainable by deficiency for a section of the fourth chromosome between and inclusive of the loci for bent and eyeless. A diminished individual is virtually haploid for this section.

The extent of a deficient region is measured in two ways: by observing to how many neighboring mapped loci pseudo-dominance extends, and by observing the amount by which the map-distance between adjacent not-included loci is decreased in the presence of the deficiency, there being no crossing over within the deficient region. The Diminished deficiency included the only two known fourth-chromosome mutants and thus made the second method impossible in this case.

(10) Exaggeration of mutants of affected section: The characters bent and eyeless in flies that are at the same time Diminished are more exrteme departures from the wild-type than are the simple bent and eyeless mutants. For example, the legs of the Diminished-bent compounds were much shorter and all the tarsi were like those of the hind legs of the most extreme normal bents; i.e., they were fused into hairy lumps instead of being chains of five slender joints. The eyes of the Diminished-eyeless compounds that hatched had about the same range as normal eyeless has; but among the dead pupae were found individuals in which the head was reduced to a mere proboscis on the end of the neck.

(11) Exaggeration of mortality of mutants of affected section: Crosses of Diminished to eyeless produced only 35 Diminished-eyeless (all males) to 2726 wild-type sibs, where equality is expected. The mortality of eye-

less in presence of Diminished is thus 98.7%. The mortality of simple eyeless is usually not greater than 5%, and the mortality of the simple Diminished is, as seen, about 47%. The mortality of Diminished-bent was even higher, viz. 99.5%, since only 9 Diminished-bents (males) hatched for 1727 wild-type sibs.

Since mortality changes must necessarily be only consequences of somatic changes, the exaggeration of the mortality of the Diminished compounds is another evidence of exaggeration of somatic changes—probably of the internal anatomy in addition to the observed superficial changes.

The mortality of Diminished, and of the Diminished compounds, is mainly due to somatic changes in the pupa stage: (*a*) If the mortality of Diminished individuals were due to changes in the larvae, then mass-cultures, because of the greater competition among the too numerous larvae, should show a lower proportion of Diminished than do sister pair cultures, but this was found not to be the case. (*b*) Examination of the culture bottles of the crosses of Diminished by eyeless showed that the number of Diminished-eyeless individuals that pupated but perished subsequently is approximately the same as the number of not-diminished flies that hatch.

(12) Exaggeration of certain mutants outside the affected region: Diminished exaggerates the third-chromosome dominant Hairless, and to a slight extent certain other mutants.

(13) Recurrent nature: Diminished has arisen independently at various times (see section II (1) below).

II. All the above features of Diminished, including exaggeration (10, 11, 12), are explainable by the theory of deficiency, and for nearly all there have been parallels in previously known cases of deficiency. Two features of Diminished appeared that made a sectional deficiency hypothesis inadequate.

(1) High frequency of re-occurrence: Diminished has been recorded some twenty-five times within the space of a year, which is too high a frequency to be explained without extreme difficulty on the sectional deficiency view. Notch-deficiencies have been recorded some 18 times, but this was in a period extending over eight years. Furthermore, there is evidence that the different Notches are not re-occurrences of the same deficiency, but show character differences and involve sections that are different in extent, though all possessing a common section in the neighborhood of facet. The different Diminished strains, on the oteher hand, are apparently identical. Most of the tests of this paper were carried out in parallel with strains No. 3, 4, 8, 15, and 3x.

(2) Exceptions to normal inheritance: In a cross of Diminished to bent there appeared a single Diminished male that was not bent. This exceptional male was tested and was found not to carry bent, although

his father had been homozygous bent. Furthermore, in a cross of Diminished to eyeless there appeared a single not-Diminished eyeless female. Genetical tests showed that this exceptional female was homozygous for eyeless, although her father had lacked eyeless entirely.

These exceptions to normal inheritance invited a comparison with the well-known exceptions to sex-linked inheritance which are due to non-disjunction of the sex chromosomes;[4] for it is evident that non-disjunction of the fourth chromosome would produce such exceptions, and also that it would give rise to the whole series of effects that are characteristic of deficiency. Diminished individuals are deficient not simply for a section of the fourth chromosome including the loci for bent and eyeless, but are deficient for a whole fourth chromosome; i.e., they are haploid for the fourth chromosome. A Diminished strain would arise from the occurrence of "primary" non-disjunction in either sex, whenever at maturation the pair of fourth chromosomes fails to disjoin and both members pass to the same pole, leaving the other pole without a fourth chromosome. Such nullo-IV eggs or sperm in union with normal haplo-IV sperm or eggs would give rise to individuals with only a single fourth chromosome. Judging by the number of independent strains of Diminished and by the two controlled exceptions, the frequency of primary non-disjunction of the fourth chromosome is of the same order as for the first.

If primary non-disjunction gave rise to nullo-IV gametes and thus to haplo-IV strains, the same process may also give rise conversely to diplo-IV gametes and thus to triplo-IV zygotes. No such individuals have as yet been indentified.[8] Aside from possible direct somatic effects of triploidy or tetraploidy for the IV chromosome, the presence of an extra chromosome would be detectable by duplication-phenomena,[9] just as the haplo-IV type was detectable by deficiency phenomena, and could be proved cytologically. The eyeless exception referred to above was produced by a diplo-IV egg, so that the process is well substantiated even here.

III. Cytological examination of the oögonial cells of Diminished individuals showed, as had been predicted, that only a single one of the small spherical chromosomes was present, while each of the other chromosomes was present in the usual paired condition. Four independent strains of Diminished, including the one that arose in the cross, were thus proved to be haploid for the fourth chromosome (fig.1).

IV. The haploid nature of the Diminished individuals made possible a back-cross determination of the bent eyeless crossover value without the necessity of a double recessive. The situation in the fourth chromosome is now comparable with that in the first, with haploidy for the fourth chromosome giving the Diminished type and pseudo-dominance of fourth-chromosome recessives, while haploidy for the first gives the male type and pseudo-dominance of sex-linked recessives. Females heterozygous for bent and for eyeless were crossed to Diminished males, and the offspring furnished the equivalent of 17 crossovers in a total of 1987, or 0.86 ± .14 per cent of crossing over.

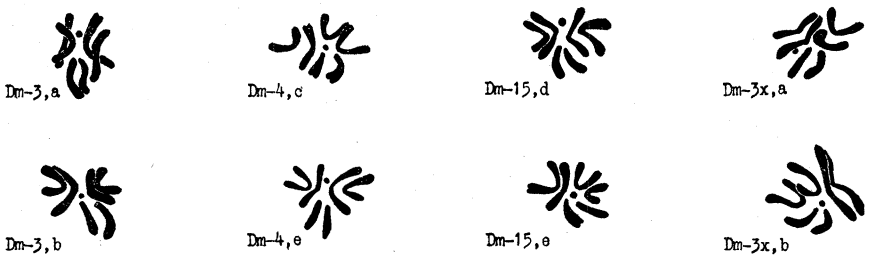

FIG. 1

An oögonial metaphase plate from each of eight "diminished" individuals, two from each of four strains, all figures showing a single round chromosome instead of the usual pair.

V. The cytological finding in the case of the haplo-fourths has put the theory of deficiency on a sound basis; for, each of the features met with in the cases described as deficiency has been met with in the case of the haplo-fourths. Thus, it has been shown, not simply that these characteristics might be produced by loss, but that in this specific case they were actually produced by loss.

VI. Both the character complex and the exaggeration effects of Diminished are due to a change in balance of the genes. Each character of the wild-type is the result of a balance between many genes that tend to modify the character in various directions. These "plus and minus modifiers" are apparently distributed at random in the chromosomes, so that if a particular short section of chromosome is removed, as in deficiencies, usually more plus than minus modifiers (or vice versa) of some character will be removed. In that case more minus than plus modifiers will remain in action, and a new character will appear, differing from the old in a minus direction.

VII. The genetic and cytological evidence in the case of Diminished has provided a positive identification of a particular chromosome—the small round one—as the carrier of the genes of particular Mendelian characters—bent and eyeless. Non-disjunction of the sex-chromosomes has previously furnished a similar identification of the rod-like chromosome as the carrier of the genes of certain sex-linked characters. Further work on non-disjunction of the X-chromosome has extended the identification to include so many sex-linked characters without exception that it may be accepted as general. Since the behavior of non-sex-linked characters had been shown to be the same as that of the sex-linked characters in a large range of particulars—in all points except those connected with the fact that the male is virtually haploid for this chromosome—the demonstration that the sex-linked genes are carried by the X-chromosome left no plausible ground for believing that that proof did not hold for the ordinary characters and the ordinary chromosomes. However, the present case offers a direct and positive identification between particular ordinary Mendelian characters and a particular autosome, so that we need no longer depend upon an extension to ordinary characters of a proof that was complete only for sex-linked characters. Taken in connection with the immense body of general proof for the chromosome theory, and with the many established parallels between hereditary behavior and chromosome behavior, these direct proofs in the case of both sex-linked and autosomal characters may be regarded as decisive.

[1] Paper read before the Genetics Seminar of the University of California, Dec., 1920.

[2] Bridges, C. B., *Genetics*, **2**, Sept., 1917 (445–465).

[3] Muller, H. J., *Jour. Exp. Zool.*, **17**, Oct., 1914 (325–537).

[4] Hoge, M. A., *Am. Nat.*, **49**, 1915 (47).

[5] Bridges, C. B., *Genetics*, **1**, Jan.–Mar., 1916 (1–52, 107–163).

[6] Bridges, C. B., *J. Gen. Physiol.*, **1**, July, 1919 (645–656).

[7] Mohr, O. L., *Genetics*, **4**, May, 1919 (275–282).

[8] Dr. Little has recently reported such an identification (*Science*, **53**, Feb. 18, 1921 (167)); but as I have pointed out in a note to *Science* (**53**, April 1, 1921 (308)) the facts as stated are more in conformity with the assumption of a "weak" allelomorph of eyeless, or of a linked dominant "minus" modifier of eyeless. (Since the above was written, triplo-fourth individuals have been identified among the offspring of triploid females (*Science*, **54**, Sept. 16, 1921 (252)).

[9] Bridges, C. B., *Proc. Am. Soc. Zool.*, 1918.

NOTE ON THE ECONOMIC CONVERSION FACTORS OF ENERGY[1]

By Alfred J. Lotka

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That there is some relation between physical energy and economic value has been more or less clearly recognized by several authors. So G. Helm, for example, conceives of an "economic energy," whose capacity factor is quantity (of commodity), and whose intensity factor is measured by the price paid per unit quantity. A certain justification for this standpoint may be found in the fact that on the one hand goods having economic value can be exchanged for, and in this sense converted into energy; while on the other hand the movement of commodities in an economic system, that is to say, the transfer of property by sale and purchase, is determined by differences in economic value in much the same way as the transfer of energy from one portion of a physical system to another is determined by differences in the intensity factor of the energy concerned in the change.